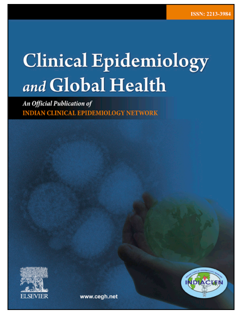
Cost-effectiveness of single-photon emission computed tomography for diagnosis of coronary artery disease: A systematic review of the key drivers and quality of published literatur...

DOI: 10.1016/j.cegh.2018.07.008

Marjan Hajahmadi
Iran University of Medical Sciences

Vahid Alipour
Iran University of Medical Sciences

Accepted Manuscript



Cost-effectiveness of single-photon emission computed tomography for diagnosis of coronary artery disease: A systematic review of the key drivers and quality of published literature

Javad Javan-Noughabi, Aziz Rezapour, Marjan Hajahmadi, Vahid Alipour

PII: S2213-3984(18)30185-4

DOI: 10.1016/j.cegh.2018.07.008

Reference: CEGH 276

To appear in: *Clinical Epidemiology and Global Health*

Received Date: 2 July 2018

Accepted Date: 20 July 2018

Cost-effectiveness of single-photon emission computed tomography for diagnosis of coronary artery disease: a systematic review of the key drivers and quality of published literature

1. Javad Javan-Noughabi,
Department of Health Economics, School of Health Management and Information Sciences, Iran University of Medical Sciences, Tehran, Iran. E-Mail: javadjavan.n@gmail.com

2. **Aziz Rezapour**,
Corresponding author: Health Management and Economics Research Center, Iran University of Medical Sciences, Tehran, Iran. E-Mail: rezapour_a57@yahoo.com, Telephone: +989122826084

3. Marjan Hajahmadi
Health Management and Economics Research Center, Iran University of Medical Sciences, Tehran, Iran

4. Vahid Alipour,
Health Management and Economics Research Center, Iran University of Medical Sciences, Tehran, Iran

Compliance with Ethical Standards:

1. Funding: This study was not supported by any funding.
2. Conflict of interest: The authors declare that they have no conflict of interest.
3. Ethical Approval: This article does not contain any studies with human participants or animals performed by any of the authors.
4. Informed Consent: For this type of study informed consent is not required.
5. Consent for publication: For this type of study consent for publication is not required.

Cost-effectiveness of single-photon emission computed tomography for diagnosis of coronary artery disease: a systematic review of the key drivers and quality of published literature

Abstract

Background: Single- photon-emission computed tomography (SPECT) being one of the most commonly used methods that significantly improved the detection of coronary artery disease. The objective of this study was to perform a systematic review of the cost-effectiveness of SPECT in diagnosis of coronary artery disease.

Methods: Electronic databases including PubMed, Scopus and Web of Science were searched from 1997 through 2017. The full economic evaluations of SPECT as the first and only test in diagnosis of coronary artery disease were included in this study. Non-English studies, conference abstracts and letters/editorials were excluded. The Consolidated Health Economic Evaluation Reporting Standards checklist was used to review the methodological quality of included studies.

Results: Eight studies met the systematic review inclusion criteria. In general, the quality of the included studies was high. The abstract of studies had the least degree of compliance with the Consolidated Health Economic Evaluation Reporting Standards checklist. The majority of the papers used decision tree model and estimated cost from a payer's perspective. This study revealed wide heterogeneity in the methodology particularly in setting, comparators, time horizon, and perspective.

Conclusion: By conducting this systematic review on 8 valid studies, it was found that the cost-effectiveness of an imaging test strongly depends on the pretest likelihood of disease. The included studies on cost-effectiveness provide conflicting evidence in support of the use of SPECT in diagnosis of coronary artery disease. This study showed that the cost-effectiveness of an imaging test varied between subgroups of patients.

Keywords: Cost-Benefit Analysis; coronary artery disease; Tomography, Emission-Computed, Single-Photon; Review

1.Introduction:

Non-communicable diseases accounted for about 60% of all deaths and 50% of the burden of disease in 2001 [1-3]. It is predicted that in 2020 both of death and global burden from Non-communicable diseases will be about 70% in developing countries [3]. Coronary Artery Disease (CAD) is one of these non-communicable disorders that will increase dramatically throughout the world by 2020 [3]. Today, CAD is the main cause of death in developed countries [4]. The prevalence of CAD and coronary risk factors in developing countries is increasing [5]. According to the important role of CAD in morbidity and death, early recognition of CAD is an essential part of public health policies [6]. Coronary Angiography (CA) is an accepted reference standard for CAD diagnosis. However, CA is expensive, and major complications occur in 1% to 2% of cases undergoing CA [7]. Thus, use of less invasive imaging tests is significant for decreasing or avoiding the Complications of CA [8]. Noninvasive tests with optimal sensitivity and specificity are developed to decide which patients should undergo coronary angiography [9]. In the past decades, various noninvasive tests for CAD diagnosis have become extensively available in clinical practice [10, 11]. Present guidelines advise the use of noninvasive imaging tests, such as Single-Photon-Emission Computed Tomography (SPECT), Positron Emission Tomographic (PET), Coronary Computed Tomographic Angiography (CCTA) and echocardiography, before coronary angiography in many people suspected of having CAD [9]. SPECT being one of the most commonly used methods that significantly improved the detection of CAD [12]. However, the effectiveness of SPECT for diagnosis of CAD is controversial [13].

The recommendations of the present guidelines for the diagnosis of CAD are not the same, and in many conditions, the adoption of a diagnosis test depend on various factors such as clinical and economic issues [10, 14]. Cost-Effectiveness Analysis (CEA) is extensively used to support decision makers to choice the best alternatives within constrained healthcare system budgets [15, 16]. It is defined as the comparative analysis of alternatives according to their costs and consequences [17]. In recent years, many of CEAs conducted on the different tests, including SPECT, for CAD diagnosis [18, 19]. Also, a systematic review has been conducted on previously published SPECT CEAs [20], but its focus has been on sensitivity and specificity of test, there has been no comprehensive assessment of the quality of these CEAs and the key drivers of cost effectiveness have not been identified. With the recent development of updated standards for economic evaluations of healthcare interventions, the main aim of this study is to perform a systematic review on the previously published studies to assess the cost-effectiveness of SPECT in diagnosis of CAD. Also, we evaluated the methodological quality of these CEAs using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist [21].

2.Methods:

We performed a systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [22].

2.1.Search Strategy:

A systematic review of the literature was performed to assess the cost-effectiveness of SPECT in diagnosis of CAD. Three electronic databases including Scopus, ISI Web of Science and PubMed for English literature published from October 1997 to October 2017 were searched. Search strategies for electronic databases were performed in accordance with Table 1.

Furthermore, references of included studies and relevant review studies manually examined for additional articles to be included.

[Insert table 1]

2.2.Study Selection:

Records were entered into EndNote 8 (Thomson Reuters, New York, NY). Duplicate reports were deleted in the first step of selection of articles. In the second stage, two authors (JJN and AR) independently examined the titles and abstracts of all search results. Articles were excluded if the study was not an economic evaluation of diagnosis strategies for CAD, or if they were conference abstracts, letters/editorials or conference reports. In the next step, the same authors independently assessed the full-text articles. Studies were included if they met the following criteria:

-Study design: Economic evaluation studies including cost effectiveness or cost utility

-population Study: patients with suspected CAD

-Outcome: Incremental Cost Effectiveness Ratio

-Screening strategies: including SPECT as the first and only test

-Languages: English

Studies with following criteria were excluded:

-Study design: conference abstracts, letters/editorials or conference reports, or not full economic evaluation of SPECT for CAD.

-population Study: patients with underlying disease such as diabetes

-Screening strategies: Several tests as a one strategy, stress SPECT, not include SPECT as the first and only test

-Languages: Non-English

Any disagreements between authors were resolved through consensus and, in cases of persistent disagreement, a third author (MH) assessed the publications. A flow chart showing the selection procedure is demonstrated in Fig. 1.

[Insert figure 1]

2.3.Data Extraction:

For each study included in the final review, data were extracted into a table. Data were extracted by JJN and confirmed by AR and MH. Again, any disagreements between authors were resolved through consensus and, in cases of persistent disagreement, a third author (VA) assessed the publications. The information obtained included authors, study year, country, comparators, decision model, cost effectiveness measure, study perspective, time horizon, sensitivity analysis, and study conclusions.

2.4.Quality Assessment of economic evaluation studies:

While there are various guidelines for economic evaluation studies [23-28], we used the CHEERS checklist because it consolidated and updated previous guidelines into a single Useful reporting standard [21, 29]. The CHEERS statement checklist developed by the ISPOR Health Economic Evaluation Publication Guidelines Task Force provides recommendations in a checklist to evaluate reporting in health economic evaluations. The aim of the CHEERS checklist is to provide recommendations to improve reporting of health economic evaluations. The CHEERS checklist contains 24 criteria assessing different aspects of quality and reporting standard of economic evaluations: background and objectives, target population and subgroups, setting and location, study perspective, comparators, time horizon, discount rate, choice of health outcomes, measurement of effectiveness, measurement and valuation of preference based outcomes, estimating resources and costs, choice of model, assumptions, analytical methods, study parameters, incremental costs and outcomes, characterizing uncertainty, characterizing heterogeneity, study findings, limitations, generalizability, source of funding, and conflicts of interest. For each included study, each checklist item was rated as ‘‘0” or ‘‘1”. Furthermore, overall quality rating of eligible studies was scored on a four-point Likert scale in a descending order of ‘‘excellent”, ‘‘good”, moderate” or ‘‘low” quality when study fulfilled 100%, >75–<100%, >50–75%, or 50% of the criteria, respectively [21, 29].

3.Results:

3.1.Study Selection:

Figure 1 show the process of literature search. Systematic database search identified 402 potentially relevant studies (PubMed: 96; Web of Science: 107; Scopus: 199). Additional records identified through other sources (n = 9). After the removal of duplicated (n = 107), 304 publications remained. Of these, 255 were rejected when the title and the abstract were reviewed and found not to be relevant. The full text of the remaining 49 publications was examined. 41 articles were excluded because they did not meet the eligibility criteria for the review (see Fig. 1). Eight studies were selected for this systematic review [18, 19, 30-35].

3.2. Quality of economic evaluation studies:

The results of the quality assessment of included CEAs according to the CHEERS checklist [21] are shown in Table 2. The quality assessment showed that the methodological quality of the included CEAs varied from 75% to 91.66%. Among the CHEERS checklist items, the abstract of articles (item 2) had the least degree of compliance with the CHEERS checklist (12.5%). 13 items including title, target population, comparators, Choice of health outcomes, Measurement of effectiveness, estimating resources and costs, Currency price date and conversion, Assumptions, Analytic methods, Study parameters, Incremental costs and outcomes, Characterizing uncertainty and finding were the most compliance with the CHEERS checklist (100%).

[Insert table 2]

3.3. Summary characteristics:

Some of the characteristics and key findings of eligible studies reported summarized in Table 3. Eight studies were selected for this systematic review [18, 19, 30-35]. The contribution of each of the continents of Asia [32, 33], Europe [18, 19] and the United States [31, 34] were two studies and two studies location were uncertain [30, 35]. Four articles provided both cost-effectiveness and cost-utility analysis [19, 33-35], while three articles performed only a cost-effectiveness [18, 31, 32] and one article conducted only a cost-utility analysis [30]. Majority of studies were conducted from the payer perspective [19, 32, 34, 35], two studies used a societal perspective [18, 30], one study conducted from health care system perspective [33] and one study perspective was uncertain [31]. Different durations of time horizon were used. Only two studies used a lifetime horizon [34, 35]. Three article used a discount rate that all of them applied rates of 3% [30, 32, 35].

[Insert table 3]

4. Discussion:

In this study, we systematically reviewed the economic evaluations of SPECT in diagnosis of CAD. Although, we found another review on SPECT CEAs [20], but the current study systematically reviewed the key drivers of cost effectiveness of SPECT in diagnosis of CAD. Also, we evaluated the methodological quality of these CEAs using the CHEERS checklist.

These items are not identified in the previous review. A comprehensive electronic and manual search found 8 economic evaluations of SPECT in diagnosis of CAD.

4.1. Quality assessment:

Included papers were assessed with CHEERS checklist. CHEERS Checklist reviewed the very detailed information of an economic evaluation study. In recent years, significant improvements have been made in the quality of economic evaluation reports. Although, none of the 8 articles included in this study could earn 100% CHEERS Checklist scores, but the quality of included studies was appropriate. Six studies were of good quality based on the CHEERS checklist [19, 30, 32-35], two studies were of moderate quality [18, 31], and none was of excellent and low. All studies completely met criteria for reporting title, target population, comparators, Choice of health outcomes, Measurement of effectiveness, estimating resources and costs, Currency price date and conversion, Assumptions, Analytic methods, Study parameters, Incremental costs and outcomes, Characterizing uncertainty and finding. Only one study met criteria for abstract [30], which could be due to limitations of journals or publications for abstract. CHEERS checklist recommended that introduction for an economic evaluation report must provide an explicit report of the broader context for the study [21]. Only three studies met this criteria [32, 33, 35]. In two studies Setting and location did not clearly state [30, 35]. Also, one study did not describe the perspective of study [31]. Five studies did not report the discount rate [18, 19, 31, 33]. One of these studies [33] used a short horizon (1 year) that did not require the use of a discount rate. However, CHEERS checklist recommended that in studies with short horizons, discount rate must described as 0% [21]. Two studies did not report the time horizon and did not used the preference-based outcomes [18, 32]. The CHEERS checklist recommended that reasons for choosing a model for study must be described and the model structure should also be represented using a figure [21]. Two studies did not met this criteria [18, 31]. CHEERS checklist for characterizing heterogeneity recommended that cost-effectiveness results explained according to variations between subgroups of patients with different baseline characteristics or other variables [21]. This item was met by six studies [18, 19, 30, 32, 33, 35]. These studies had a subgroup analysis according to Pretest Likelihood of Disease (PLD). One study also explained cost effectiveness results based on age and sex [30]. Three studies did not describe any potential for conflicts of interest of study contributors [30, 32, 35]. One study did not clearly state the funding sources [32].

4.2. Cost-Effectiveness:

By conducting this systematic review on 8 valid studies, it was found that the cost-effectiveness of an imaging test strongly depends on the PLD.

Cost-effectiveness considerations suggest that echocardiography, SPECT, and immediate angiography are the most appropriate diagnostic tests for patients at intermediate pretest risk for having coronary disease. At a 25% prevalence of disease, echocardiography seems to be the most attractive test under most circumstances; SPECT would be chosen over echocardiography only if a cost-effectiveness ratio of $110 000 is considered acceptable, and immediate angiography would be chosen over SPECT only at a cost-effectiveness ratio of $355 000. Thus, echocardiography remains a cost-effective strategy at a wide range of prevalence of disease, whereas immediate angiography is a cost-effective choice when the pretest probability of disease is high [30]. The results of another study indicated that imaging modalities that include cardiac CCTA are the most cost-effective methods in symptomatic patients with suspected obstructive CAD and a PLD of ≤50%. In high-risk patients (PLD > 50%), immediate Invasive coronary angiography (CATH) appears to be the most cost-effective strategy. This study showed that ischemia imaging techniques (SPECT and Stress Echo) are more expensive and less effective compared with other diagnostic strategies for all assessed PLDs [18]. In another study, The cost-effectiveness acceptability curves from the probabilistic sensitivity analysis showed that at 30% and 50% CAD prevalence or the coronary CT angiography–first or coronary CT angiography–only strategy was the most cost-effective up to the threshold level of $50 000 per QALY. At a higher CAD prevalence of 80%, however, the invasive coronary angiography approach was the most cost-effective strategy, with an ICER of $7994.36 relative to the coronary CT angiography–only approach. Coronary CT angiography–first and coronary CT angiography–only strategies remained dominant up to a baseline coronary CT angiography test cost of $1100 and 80% CAD prevalence [35]. The results of some included studies showed that the SPECT is a dominated strategy in CAD diagnosis. One study compared cost-effectiveness of Dual-Energy Computed Tomography (DECT) versus of SPECT for diagnosis of CAD. This study showed that compared to SPECT, DECT was dominant strategy [34]. Another study that conducted cost effectiveness of MRI and SPECT in CAD found that for patients with any pre-test likelihood of CAD, p-MRI was a cost-effective strategy in the comparison of SPECT [32]. In comparison of SPECT and cardiovascular magnetic resonance (CMR), showed that CMR has relatively better cost-effectiveness and utility across all prevalence levels and the full range of sensitivity analyses [19]. However, SPECT was dominant versus Positron-Emission Tomography (PET). Hlatky et al compared the cost-effectiveness of coronary computed tomography angiography (CTA), PET and SPECT in diagnosis of CAD. They resulted that SPECT has better cost-effectiveness compared with PET, whereas CTA was associated with higher costs and no significant difference in mortality compared with SPECT [31]. Another study was conducted a Cost-effectiveness of SPECT against CCTA using test accuracy and quality-adjusted life year (QALY). In the model using diagnostic accuracy, CCTA was more effective and less expensive than SPECT ($725.38 for CCTA vs. $661.46 for SPECT). In the model using QALY, CCTA was generally more effective in terms of life quality (0.00221 QALY) and cost ($513) than SPECT. However, cost utility varied among subgroups, with SPECT outperforming CCTA in patients with a pretest probability of 30% to 60% (0.01890 QALY; $113) [33].

There are several limitations in this systematic review including the exclusion of unpublished manuscripts and abstracts from conference proceedings.

5. Conclusion:

This study provides a valuable information on the key drivers and trends in cost effectiveness of SPECT in CAD diagnosis for decision makers and stakeholders. Due to heterogeneity in the methodology (comparators, time horizon, and perspective) and data sources (effectiveness and costing data) of CEAs, no synthesis of the data was possible. Instead, we summarized key drivers and major finding of CEAs. The included studies on cost-effectiveness provide conflicting evidence in support of the use of SPECT in diagnosis of CAD. This study showed that the cost-effectiveness of an imaging test varied between subgroups of patients such as PLD, sex and age. CHEERS checklist recommended that cost-effectiveness results explained adhere to variations between subgroups of patients with different baseline characteristics or other variables. While the quality of the included CEAs was generally high, some of the CEAs could not provide all the detailed evidence required by the CHEERS checklist. If allowed by journal or publication restrictions, next CEAs should adhere to standard reporting guidelines, such as CHEERS, so that readers can assess and compare the quality of study results.

Funding:

No funding was received for the conduct of this study.

Conflict of interest:

The authors declare that there is no conflict of interest.

References:

1. Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. The Lancet. 2006;367(9524):1747-57.

2. Ghaffar A, Reddy KS, Singhi M. Burden of non-communicable diseases in South Asia. BMJ: British Medical Journal. 2004;328(7443):807.

3. Boutayeb A, Boutayeb S. The burden of non communicable diseases in developing countries. International journal for equity in health. 2005;4(1):2.

4. Daly CA, De Stavola B, Sendon JLL, Tavazzi L, Boersma E, Clemens F, et al. Predicting prognosis in stable angina—results from the Euro heart survey of stable angina: prospective observational study. Bmj. 2006;332(7536):262-7.

5. Reddy KS. Cardiovascular disease in non-Western countries. New England Journal of Medicine. 2004;350(24):2438-40.

6. Vos T, Barber R, Bell B, Bertozzi-Villa A, Biryukov S, Bolliger I, et al. Global Burden of Disease Study 2013 Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2015;386(9995):743-800.

7. Cuocolo A, Acampa W, Imbriaco M, De Luca N. The many ways to myocardial perfusion imaging. The quarterly Journal of Nuclear Medicine and Molecular Imaging. 2005;49(1):4.

8. Johnson LW, Krone R. Cardiac catheterization 1991: a report of the Registry of the Society for Cardiac Angiography and Interventions (SCA&I). Catheterization and Cardiovascular Interventions. 1993;28(3):219-20.

9. Gibbons RJ, Abrams J, Chatterjee K, Daley J, Deedwania PC, Douglas JS, et al. ACC/AHA 2002 guideline update for the management of patients with chronic stable angina—summary article. Circulation. 2003;107(1):149-58.

10. Fihn SD, Blankenship JC, Alexander KP, Bittl JA, Byrne JG, Fletcher BJ, et al. 2014 ACC/AHA/AATS/PCNA/SCAI/STS focused update of the guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, and the American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. The Journal of Thoracic and Cardiovascular Surgery. 2015;149(3):e5-e23.

11. Skinner JS, Smeeth L, Kendall JM, Adams PC, Timmis A. NICE guidance. Chest pain of recent onset: assessment and diagnosis of recent onset chest pain or discomfort of suspected cardiac origin. Heart. 2010;96(12):974-8.

12. Mastouri R, Sawada SG, Mahenthiran J. Current noninvasive imaging techniques for detection of coronary artery disease. Expert review of cardiovascular therapy. 2010;8(1):77-91.

13. Burrell S, MacDonald A. Artifacts and pitfalls in myocardial perfusion imaging. Journal of nuclear medicine technology. 2006;34(4):193-211.

14. Cooper A, Timmis A, Skinner J. Assessment of recent onset chest pain or discomfort of suspected cardiac origin: summary of NICE guidance. BMJ: British Medical Journal. 2010;340.

15. Boudreau R, Blackhouse G, Goeree R, Mierzwinski-Urban MA. alefacept, efalizumab, etanercept, and infliximab for severe psoriasis vulgaris in adults: budget impact analysis and review of

comparative clinical-and cost-effectiveness [Technology Report no 97]. Ottawa: Canadian Agency for Drugs and Technologies in Health; December 2007. Technology report. 2008(97).

16. Mauskopf J, Samuel M, McBride D, Mallya UG, Feldman SR. Treatment sequencing after failure of the first biologic in cost-effectiveness models of psoriasis: a systematic review of published models and clinical practice guidelines. Pharmacoeconomics. 2014;32(4):395-409.

17. Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. Methods for the economic evaluation of health care programmes: Oxford university press; 2015.

18. Ferreira AM, Marques H, Gonçalves PA, Cardim N. Cost-effectiveness of different diagnostic strategies in suspected stable coronary artery disease in Portugal. Arquivos brasileiros de cardiologia. 2014;102(4):391-402.

19. Boldt J, Leber AW, Bonaventura K, Sohns C, Stula M, Huppertz A, et al. Cost-effectiveness of cardiovascular magnetic resonance and single-photon emission computed tomography for diagnosis of coronary artery disease in Germany. Journal of cardiovascular magnetic resonance. 2013;15(1):30.

20. Trägårdh E, Tan SS, Bucerius J, Gimelli A, Gaemperli O, Lindner O, et al. Systematic review of cost-effectiveness of myocardial perfusion scintigraphy in patients with ischaemic heart disease: A report from the cardiovascular committee of the European Association of Nuclear Medicine. Endorsed by the European Association of Cardiovascular Imaging. European Heart Journal–Cardiovascular Imaging. 2017:jex095.

21. Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, et al. Consolidated health economic evaluation reporting standards (CHEERS) statement. Cost Effectiveness and Resource Allocation. 2013;11(1):6.

22. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS medicine. 2009;6(7):e1000097.

23. Drummond M, Jefferson T. Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. BMJ: British Medical Journal. 1996;313(7052):275.

24. Hilman A. Task force on principles for economic analysis of health care technology: Economic analysis of health care technology: A report on principles. Ann Intern Med. 1995;123:61-70.

25. Ramsey S, Willke R, Briggs A, Brown R, Buxton M, Chawla A, et al. Good research practices for cost-effectiveness analysis alongside clinical trials: the ISPOR RCT-CEA Task Force report. Value in health. 2005;8(5):521-33.

26. Siegel JE, Weinstein MC, Russell LB, Gold MR. Recommendations for reporting cost-effectiveness analyses. Jama. 1996;276(16):1339-41.

27. Davis J, Robertson MC, Comans T, Scuffham P. Guidelines for conducting and reporting economic evaluation of fall prevention strategies. Osteoporosis international. 2011;22(9):2449-59.

28. Goetghebeur MM, Wagner M, Khoury H, Levitt RJ, Erickson LJ, Rindress D. Evidence and Value: Impact on DEcisionMaking–the EVIDEM framework and potential applications. BMC health services research. 2008;8(1):270.

29. Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, et al. Consolidated health economic evaluation reporting standards (CHEERS)—explanation and elaboration: a report of the ISPOR health economic evaluation publication guidelines good reporting practices task force. Value in Health. 2013;16(2):231-50.

30. Garber AM, Solomon NA. Cost-effectiveness of alternative test strategies for the diagnosis of coronary artery disease. Annals of internal medicine. 1999;130(9):719-28.

31. Hlatky MA, Shilane D, Hachamovitch R, DiCarli MF, Investigators S. Economic outcomes in the study of myocardial perfusion and coronary anatomy imaging roles in coronary artery disease registry: the SPARC study. Journal of the American College of Cardiology. 2014;63(10):1002-8.

32. Iwata K, Ogasawara K. Comparison of the cost-effectiveness of stress myocardial perfusion MRI and SPECT in patients with suspected coronary artery disease. Radiological physics and technology. 2013;6(1):28-34.

33. Lee S-P, Jang EJ, Kim Y-J, Cha M-J, Park S-Y, Song HJ, et al. Cost-effectiveness of coronary CT angiography in patients with chest pain: comparison with myocardial single photon emission tomography. Journal of cardiovascular computed tomography. 2015;9(5):428-37.

34. Meyer M, Nance JW, Schoepf UJ, Moscariello A, Weininger M, Rowe GW, et al. Cost-effectiveness of substituting dual-energy CT for SPECT in the assessment of myocardial perfusion for the workup of coronary artery disease. European journal of radiology. 2012;81(12):3719-25.

35. Min JK, Gilmore A, Budoff MJ, Berman DS, O'Day K. Cost-effectiveness of coronary CT angiography versus myocardial perfusion SPECT for evaluation of patients with chest pain and no known coronary artery disease. Radiology. 2010;254(3):801-8.

Table 1: Search strategies for PubMed, Scopus and ISI

Database	Search Strategy
PubMed	("Cost-Benefit Analysis" [MeSH] OR "Economic evaluation" [tiab] OR "Cost effectiveness" [tiab] OR "Cost-benefit" [tiab] OR "Cost-utility" [tiab]) AND ("Tomography, Emission-Computed, Single-Photon" [MeSH] OR "single Photon Emission Computed Tomography" [tiab] OR spect[tiab]) AND ("coronary artery disease" [MeSH] OR "coronary artery disease" [tiab])
Scopus	TITLE-ABS-KEY("Cost-Benefit Analysis" OR "Economic evaluation" OR "Cost effectiveness" OR "Cost-benefit" OR "Cost-utility") AND TITLE-ABS-KEY("Tomography, Emission-Computed, Single-Photon" OR "single Photon Emission Computed Tomography" OR spect) AND TITLE-ABS-KEY("coronary artery disease")
ISI	1. "Cost-Benefit Analysis" OR "Economic evaluation" OR "Cost effectiveness" OR "Cost-benefit" OR "Cost-utility" 2. "Tomography, Emission-Computed, Single-Photon" OR "single Photon

	Emission Computed Tomography" OR spect 3. "coronary artery disease" 4. 1 And 2 AND 3

Table 2: Quality of the included studies using CHEERS checklist

Item no.	Section/item	Ferreira [18]	Boldt [19]	Lee [33]	Hlatky [31]	Meyer [34]	Garber [30]	Min [35]	Iwata [32]	Overall
1	Title	1	1	1	1	1	1	1	1	%100
2	Abstract	0	0	0	0	0	1	0	0	%12.5
3	Background and objectives	0	0	1	0	0	0	1	1	%37.5
4	Target population and subgroups	1	1	1	1	1	1	1	1	%100
5	Setting and location	1	1	1	1	1	0	0	1	%75
6	Study perspective	1	1	1	0	1	1	1	1	%87.5
7	Comparators	1	1	1	1	1	1	1	1	%100
8	Time horizon	0	1	1	1	1	1	1	0	%75
9	Discount rate	0	0	0	0	0	1	1	1	%37.5
10	Choice of health outcomes	1	1	1	1	1	1	1	1	%100
11	Measurement of effectiveness	1	1	1	1	1	1	1	1	%100
12	Measurement and valuation of preference-based outcomes	0	1	1	1	1	1	1	0	%75
13	Estimating resources and costs	1	1	1	1	1	1	1	1	%100
14	Currency, price date, and conversion	1	1	1	1	1	1	1	1	%100
15	Choice of model	0	1	1	0	1	1	1	1	%75
16	Assumptions	1	1	1	1	1	1	1	1	%100
17	Analytic methods	1	1	1	1	1	1	1	1	%100
18	Study parameters	1	1	1	1	1	1	1	1	%100
19	Incremental costs and outcomes	1	1	1	1	1	1	1	1	%100
20	Characterizing uncertainty	1	1	1	1	1	1	1	1	%100
21	Characterizing heterogeneity	1	1	1	0	0	1	1	1	%75
22	Study findings, limitations, generalizability, and current knowledge	1	1	1	1	1	1	1	1	%100
23	Source of funding	1	1	1	1	1	1	1	0	%87.5
24	Conflicts of interest	1	1	1	1	1	0	0	0	%62.5
	Overall quality	%75	%87.5	%91.66	%75	%83.33	%87.5	%87.5	%79.16	

Table 3: key drivers and major finding of the included studies

Author	**year**	**Country**	**Imaging modalities**	**Model**	**Cost-Effectiveness Measure**	Study perspective	Time horizon	**Major findings**
António Miguel Ferreira [18]	2013	Portugal	ET-MPS ET-CCTA SPECT StressEcho CCTA CACS-CCTA CATH	decision-making tree Bayesian inference	cost per correct diagnosis	society's perspective		Diagnostic algorithms that include cardiac computed tomography angiography are the most cost-effective in symptomatic patients with suspected stable coronary artery disease and a pretest likelihood of disease of ≤50%. In high-risk patients (pretest likelihood of disease ≥ 60%), up-front invasive coronary angiography appears to be the most cost-effective strategy. In all pretest likelihoods of disease, strategies based on ischemia appear to be more expensive and less effective compared with those based on anatomical tests.
Julia Boldt [19]	2013	Germany	CMR SPECT invasive coronary angiography	Bayes' theorem	cost per accurate diagnosis of CAD cost per quality-adjusted life-years gained (ΔQALY)	health care payer's perspective	10 y	In patients with low to intermediate pretest probabilities, CMR is more cost-effective for the detection of CAD than SPECT. The superior diagnostic accuracy of CMR also leads to an improved clinical utility as indicated by lower costs per number of QALYs gained. Above a threshold value of CAD prevalence of 0.60, proceeding directly to invasive angiography was found to be the most cost-effective diagnostic strategy.
Seung-Pyo Lee	2015	Korea	CCTA SPECT	decision tree	cost per accurate	health care system	1 y	In the model using diagnostic accuracy, CCTA was more effective

[33]			CAG		diagnosis of CAD cost per quality-adjusted life-years gained (ΔQALY)	perspective		and less expensive than SPECT ($725.38 for CCTA vs $661.46 for SPECT). In the model using QALY, CCTA was generally more effective in terms of life quality (0.00221 QALY) and cost ($513) than SPECT. However, cost utility varied among subgroups, with SPECT outperforming CCTA in patients with a pretest probability of 30% to 60% (0.01890 QALY; $113).
Mark A. Hlatky [31]	2014	United States & Canada	CTA SPECT PET	multivariable analysis	Cost per life-year added	N/A	2 y	SPECT was economically attractive compared with PET, whereas CTA was associated with higher costs and no significant difference in mortality compared with SPECT.
Mathias Meyer [34]	2012	United States	DECT SPECT	Monte Carlo simulation model	Cost per correct diagnose cost per QALY	payer perspective	Lifetime	SPECT was significant less effective if compared to DECT with an ICER of $3557 per QALY (p=0.0004) and $3625 per correct diagnose (p=0.0001).
Alan M. Garber [30]	1999	-	Angiography PET SPECT Echo Planar thallium imaging Exercise electrocardiography	decision tree Markov Model	costs per QALY	Societal perspective	30 y	Cost-effectiveness considerations suggest that echocardiography, SPECT, and immediate angiography are the most appropriate diagnostic tests for patients at intermediate pretest risk for having coronary disease.
James K. Min [35]	2010	Payers perspective	CCTA SPECT	Markov Model	cost per correct diagnosis	payer perspective	Lifetime	With a $20 000 threshold level for cost per correct diagnosis and $50 000 per QALY, a coronary CT angiography–only approach is the most cost-

					costs per QALY			effective diagnostic strategy for evaluation of patients who have stable chest pain without known CAD with intermediate CAD prevalence.
Kunihiro Iwata [32]	2012	Japan	MRI SPECT	Decision tree model	Cost per correct diagnosis	payer's perspective		For outpatients with chest pain, p-MRI had good clinical effectiveness and cost-effectiveness compared with SPECT. In the management of patients with suspected CAD, p-MRI is as useful as SPECT.

ET-MPS: Ergometric test followed by myocardial perfusion scintigraphy
ET-CCTA: Ergometric test followed by cardiac computed tomography angiography
CACS-CCTA: calcium scoring followed by cardiac computed tomography angiography
CCTA: cardiac computed tomography angiography
SPECT: single photon emission computed tomography
CATH: invasive coronary angiography
CMR: cardiovascular magnetic resonance
CAG: Coronary angiography
CTA: coronary computed tomography angiography
PET: positron-emission tomography
DECT: dual-energy computed tomography
MRI: magnetic resonance imaging

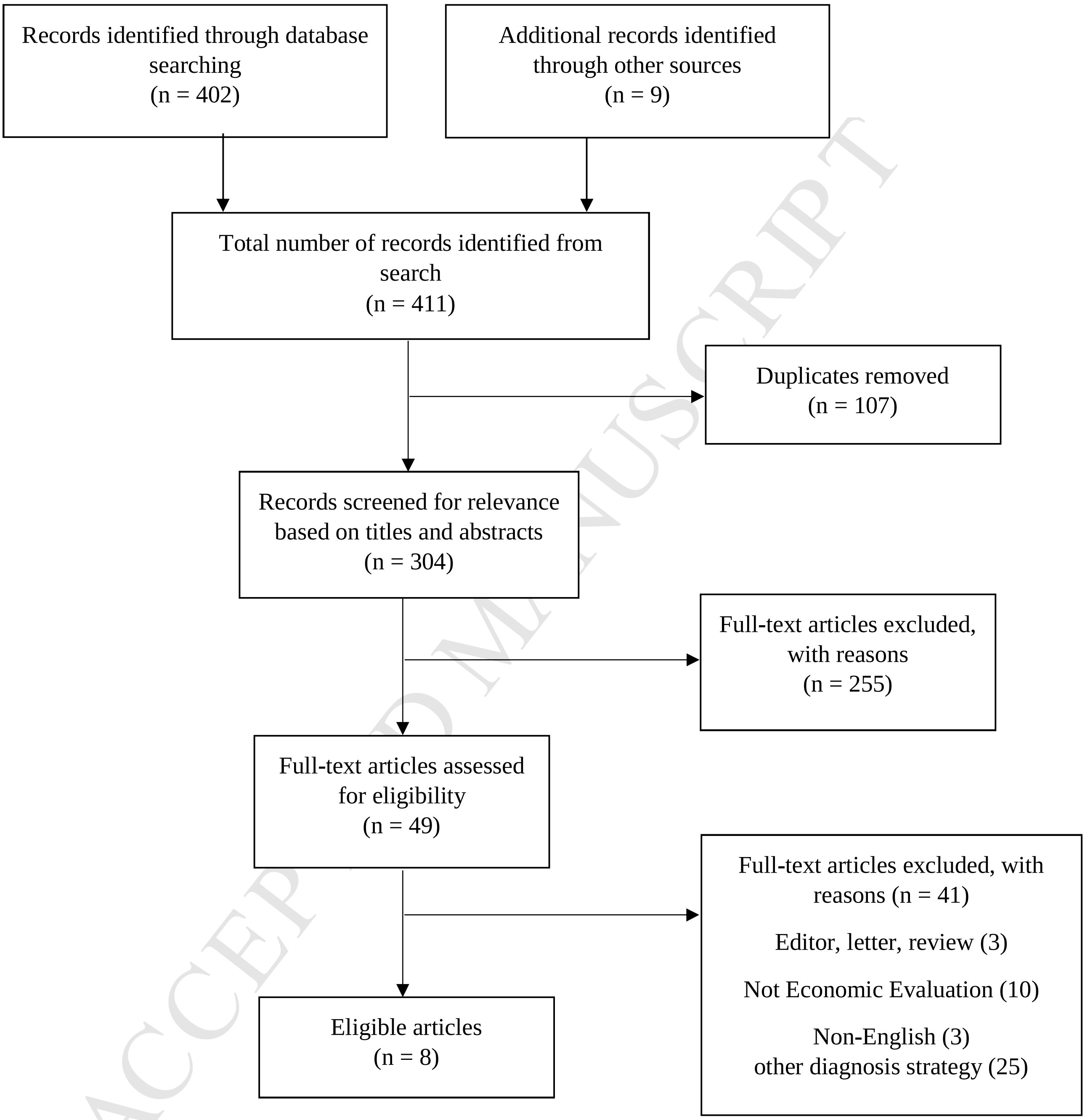


Figure 1: PRISMA flow diagram of the selection process used to identify studies for inclusion in this review.